

REMARKS

Formal Matters

Claims 37 to 44 were examined and rejected.

Claims 37 and 38 are amended for clarity. No new matter is added.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

New Matter Rejections

Claims 37-44 are rejected as failing to meet the written description requirement of 35 U.S.C. § 112, first paragraph. This is a new matter rejection. Applicants respectfully traverse.

The written description requirement of 35 U.S.C. § 112, first paragraph, involves the question of whether the subject matter of a claim conforms to the disclosure of an application as filed. According to the MPEP, an objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed?"¹ The subject matter of the claim need not be described literally (i.e. using the same terms or *in haec verba*) in order for the disclosure to satisfy the written description requirement. Likewise, MPEP states that newly added claim limitations may be supported by disclosure that is express, implicit, or inherent.²

In the prior response, the Applicants identified where support for new claims 37-44 can be found in the instant patent application and in parent application 09/062,330 (now 6,897,031).

In this Office Action, the Examiner argues that the new claims introduce new matter into the application. Each issue raised by the Examiner is set forth under a separate header below.

¹ See MPEP § 2163.02, citing *In re Gosteli* 872 F.2d 1008, 1012 (Fed. Cir. 1989).

² MPEP § 2163: "The written description requirement prevents an applicant from claiming subject matter that was not adequately described in the specification as filed. New or amended claims, which introduce elements or limitations, which are not supported by the as-filed disclosure, violate the written description requirement... While there is no *in haec verba* requirement, **newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure.** (emphasis added)

Disparate support

On page 3 of the Office Action, the Examiner argues claim 37 of the instant application contains new matter because the claim “in its entirety (as a unit) is not supported in the as-filed application”. On page 4 of the Office Action, the Examiner states that “Applicants cite disparate sections of the specification provided support for individual method steps or components recited in the general support of claim 37”. In making the rejection, the Examiner provides an example of an application having claims that are supported in one contiguous section of the application (“Cf. with the claims of the parent issued patent US 6,897,031 (*031 patent) which finds support in its entirety in specification at e.g., col. 2, lines 22-35”; see OA, sentence bridging pages 3 and 4). Because support for the claims is disparate, the Examiner concludes that the claims are not supported.

However, support for a claim need not be in one place in the specification. See, e.g., MPEP § 2163.05. Since the Examiner has not cited any authority to support her assertion that support for a claim needs to be in one place in the specification (as a unit) and the Applicants cannot find any requirement for such, the Applicant submits the Examiner’s comments in this section carry no weight.

In view of the foregoing discussion, this part of the rejection may be withdrawn.

Mammalian cells grown in vitro

On page 4 of the Office Action, the Examiner states that there is nothing in the cited section that “recites for mammalian cells grown *in vitro*” and also that “the 10³ refers to a library of cells and not to a library of 10³ vectors”.

That the method can be done using mammalian cells is explicitly described on page 10, line 20, of the instant application:

Preferred cell types for use in the invention will vary with the cellular phenotype to be modulated. Suitable cells include, but are not limited to, mammalian cells, including animal (rodents, including mice, rats, hamsters and gerbils), primates, and human cells, particularly including tumor cells of all

That the method can be done using cells grown *in vitro* is explicitly described at page 10, lines 10-14 of the instant specification:

10^6 to 10^9 being especially preferred. The population or sample can contain a mixture of different cell types from either primary or secondary cultures although samples containing only a single cell type are preferred, for example, the sample can be from a cell line, particularly tumor cell lines (particularly when, as outlined below. The cells may be in any cell phase, either synchronously or not, including M,

That the method can be done using a library of at least 10^3 vectors is implicitly supported at page 10, lines 8-10:

By a "population of cells" or "library of cells" or "plurality of cells" herein is meant at least two cells, with at least about 10^3 being preferred, at least about 10^6 being particularly preferred, and at least about 10^8 to 10^9 being especially preferred. The population or sample can contain a mixture of different cell in combination with page 21 lines 1-2, which states that in certain cases the target cells contain a single vector:

In addition, it is possible to configure a retroviral vector to allow inducible expression of retroviral inserts after integration of a single vector in target cells; importantly, the entire system is contained within the single retrovirus. Tet-inducible retroviruses have been designed incorporating the Self-

If there are at least 10^3 cells each containing a single vector, then there is implicit support for 10^3 vectors.

Applicants further note that the introduction of libraries of agents of various complexities into a population of cells is discussed on page 19 of the specification. Since there may be at least 10^3 cells, it follows that there may be 10^3 vectors.

Based on the above, the phrase "at least 10^3 vectors encoding different candidate agents into a population of mammalian cells grown *in vitro*" is fully supported in the instant application.

In view of the foregoing discussion, this part of the rejection may be withdrawn.

Physiological signals

On pages 5 and 6 of the Office Action, the Examiner states that "subjecting" a population of cells to a physiological signal is not supported because the specification only recites "evaluating" cells in the presence of absence of a physiological signal.

Evaluating cells in the presence or absence of a physiological signal implicitly requires that the cells are subjected to a physiological signal. As such, "subjecting" a population of cells to a physiological signal is implicitly supported in the specification.

In view of the foregoing discussion, this part of the rejection may be withdrawn.

At least three optical properties

On pages 6 and 7 of the Office Action, the Examiner argues that support for “at least three optical properties” as claimed is not provided by the cited support (which recites “at least three, four or five cellular parameters”).

However, the cellular parameters by which a cell is sorted are in fact optical properties. See, e.g., the entire application particularly the context given on page 34, lines 30-37, which states that the characteristics of a cell can be measured by light scatter properties. Moreover, in the flow cytometry arts (and consistent with how the term is used in the instant application) a “parameter” corresponds to an optical property (e.g., fluorescence, side scattering, etc.).

In view of the above, the Applicants submit that the cited support (which recites “at least three, four or five cellular parameters”) provides more than adequate support for the phrase “at least three optical properties” as claimed.

In view of the foregoing discussion, this part of the rejection may be withdrawn.

Sequencing to identify

The Examiner states that the cited passage on page 28, lines 10-12 does not provide support for the last element of the claims, i.e., sequencing the nucleic acid. Supplemental support for this element is found on page 32, lines 34-36, as shown below.

In a preferred embodiment, the bioactive agent is characterized. This will proceed as will be appreciated by those in the art, and generally includes an analysis of the structure, identity, binding affinity and function of the agent. Generally, once identified, the bioactive agent is resynthesized and

Applicants submit that because the structure of a nucleic acid is defined by its nucleotide sequence, the “analysis of the structure” of a nucleic acid provides implicit support for sequencing the nucleic acid.

In view of the foregoing discuss, the Applicants submit that the Examiner has no reason to reject the claims as containing new matter. Withdrawal of this rejection is therefore requested.

Rejection of claims under 35 U.S.C. § 112, 1st paragraph (written description)

In addition to the new matte rejection discussed above, claims 37-44 are also rejected as failing to meet the written description requirement of 35 U.S.C. § 112, first paragraph. Applicants respectfully traverse.

With respect to satisfying the written description requirement, even in an “unpredictable art,” applicants “are *not* required to disclose *every* species encompassed by their claims . . .”³ Otherwise, to claim a genus, every species within a genus would have to be explicitly described. This is not the law. In other words, the written description requirement does not require a specific description of every species encompassed by a claim.

Furthermore, the Written Description Guidelines (Federal Register Vol. 66 No. 4, dated January 5, 2001), using no uncertain terms, state that the specification of a patent application need only described in detail that which is new or not conventional.

For example, on page 1105 of the Guidelines it is stated: “The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of skill in the art”

Also, on page 1105 of the Guidelines it is stated: “Information which is well known in the art need not be described in detail in the specification”

On page 1106, the Guidelines state: “The description need only describe in detail that which is new or not conventional” and “What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail”.

This rejection is largely based on whether a library of 10^3 vectors encoding different candidate agents are adequately described. See, e.g., “The specification at the time of filing does not describe a library 10^3 vectors” (p. 9), “It does not describe all or any kinds of vectors” (p. 9), “there is no description of a candidate agent that has been isolated or identified” (p. 9), “the specification reference is made . . . not to a 10^3 library that encodes an enormous numbers of different kinds of candidate agents” (p. 10), “Nor is there a description of the candidate agents that alters any or all kinds of phenotypes” (p. 10), “There are no characterizing features of the genus candidate agent coupled with a functional limitation or core sequences” (p. 10). Applicants traverse.

³ *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. (BNA) 214, 218, (C.C.P.A. 1976).

Libraries of vectors are generically described in the instant specification at, e.g., page 19, line 31 to page 21, line 11. Moreover, libraries of vectors are conventional in the art (see, e.g., Nolan / WO 97/27212), which is cited by the Examiner in an obviousness rejection that is discussed below.

Thousands of other publications describe the production and use of libraries of vectors. Since the guidelines clearly state that “the description need only describe in detail that which is new or not conventional” and “What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail”, there is no need for the Applicants to provide a detailed description of libraries of vectors that can be used in the rejected claims. Moreover, the candidate agents recited in the claims are not required to perform any specific function or to have any particular structure. There is no need to describe the specific function or particular structure of something that does not need a specific function or particular structure to work.

Withdrawal of this rejection is therefore requested.

Rejection of claims under 35 U.S.C. § 112, 1st paragraph (enablement)

Claims 37-44 are rejected as failing to meet the enablement requirement of 35 U.S.C. § 112, first paragraph. Applicants respectfully traverse.

The law relating to enablement is well established.

When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by the claim is not adequately enabled by the description of the invention provided in the specification of the application.

In re Wright, 999 F.2d 1557, 1561-62 (Fed. Cir. 1993)

“[T]he question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation ‘must not be unduly extensive’”.

PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564 (Fed. Cir. 1996)

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

PPG Indus., 75 F.3d 1564 (quoting *Ex parte Jackson* 217 USPQ 804 807 (BPAI 1982))

Factors to be considered in determining whether a disclosure would require undue experimentation . . . include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1998).

Like the written description rejection addressed above, this rejection is based on whether one of skill in the art can make and use a library of vectors encoding candidate agents. In making the rejection, the Examiner states that “The specification fails to give adequate direction and guidance in how to make the 10^3 library of vectors” (p. 12, lines 8-9) and “Applicants have failed to provide any working examples for a 10^3 library of any kind of vectors” (page 12 lines 17-18).” And “The state of the prior art is such that the consequences of some bioactive agents and cell interaction on some cells have not yet been fully determined or elucidated” (p. 13 lines 6-8) and, while acknowledging that the level of skill in the art is high, the Examiner states that “the molecular library and gene art is so unpredictable that it would require undue experimentation to make the invention. Examiner states that a “candidate bioactive agent” is an example of what is unpredictable. See p. 14 lines 9-11.

The Examiner is requested to apply the arguments in the prior section of this response to this rejection. Specifically, the Applicants submit that libraries of vectors are conventional in the art and, as such, their making and use does not require undue experimentation. Moreover, the candidate agents recited in the claims are not required to perform any specific function or to have any particular structure. There is no need to describe the specific function or particular structure of something that does not need a specific function or particular structure to work.

The Applicants submit that this rejection has been adequately addressed. Withdrawal of this rejection is requested.

Rejection of claims under 35 U.S.C. § 112, 2nd paragraph

Claims 37-44 are rejected as failing to meet the enablement requirement of 35 U.S.C. § 112, second paragraph.

The MPEP states that one of the requirements set forth in 35 U.S.C. § 112, second paragraph is that the claims must particularly point and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant. This requirement is an objective one and is evaluated in the context of “whether the claim is definite - i.e., whether the scope of the claim is clear to a hypothetical person possessing the ordinary level of skill in the pertinent art.” (see MPEP § 2171). Breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971). If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. § 112, second paragraph. (see MPEP § 2173.04).

Each part of this rejection is respectfully traversed below.

No nexus

Claim 37 is rejected because the steps of the claim allegedly lack a nexus. Specifically, the Examiner believes that the claim lacks a nexus because it is not clear whether a physiological signal is similarly applied in the presence of a candidate agent.

The Applicants submit that the Examiner is mis-reading claim 37. The first step of claim 37 requires introducing candidate agents into a population of cells. The second step of claim 37 requires subjecting the population of cells to a physiological signal. As characterized in the second step of claim 37, the physiological signal is one that stimulates a phenotype in the cells in the absence of the candidate bioactive agents. Thus, the plain wording of claim 37 makes it clear that the physiological signal is applied in the presence of a candidate agent.

The Applicants submit the Examiner has no valid reason to argue that claim 37 does not contain a nexus. As such, this rejection should be withdrawn.

Inconsistency with the disclosure; the vector encodes the agent

Claim 37 is rejected because it recites “at least 10^3 vectors” and, as such, is allegedly inconsistent with the disclosure. As best understood by the Applicants, the Examiner believes that the claim is confusing because “the specification teaches a library of 10^3 cells not vectors”.

Unless the specification contains an ambiguous definition of a claim term, it is the wording of the claim itself that determines whether the claim is definite. In this case, the term “at least 10^3 vectors” is unambiguous and, as such, the Examiner has no basis for this rejection. The claims cannot automatically be indefinite because the Examiner believes that they contain new matter.

Moreover, the Examiner further argues that it is unclear whether the vector itself is encoding the candidate agent. Again, claim 37 recites “a library of at least 10^3 vectors encoding different candidate agents”. It is not clear how the Examiner can question whether the vectors encode the candidate agents when the claims explicitly require that they do.

Preamble

Claim 37 is rejected as having an incomplete preamble. The Examiner questions whether the method is a method for method is of screening for cells or a method of screening for candidate agents.

In response, the Applicants respectfully submit that there is nothing in the MPEP or current law that requires that the preamble of a claim and the final step of the claim must agree. In fact, as set forth in MPEP § 2111.01⁴, reciting the purpose or intended use of a claimed method (e.g., whether a method is for screening cells or candidate agents, for example) is “not considered a limitation and is of no significance to claim construction”. Accordingly, there is no need to amend the claim so as to further clarify the intended use/purpose of the claim: such an amendment would carry no weight and would have no significance, according to the MPEP.

The use of the word “type”

Claim 37 is rejected as reciting the word “type”. The Examiner believes that this word renders the claim indefinite because it is not clear “what manner the cells are considered of the same “type””.

Without any intention to acquiesce to the correctness of this rejection, claim 37 has been amended to remote the term “type”.

As such, this part of the rejection has been addressed and may be withdrawn.

The use of the word “the”

Claim 37 is rejected for reciting the word “the”, as in “in the absence of the candidate bioactive agents”, “the basis of at least three” and “the nucleic acid”.

To comply with § 112, ¶ 2, a claim must “particularly point[] out and distinctly claim[] the subject matter which the applicant regards as his invention.” The courts has stated that “[c]laims are considered indefinite when they are ‘not amenable to construction or are insolubly ambiguous Thus, the definiteness of claim terms depends on whether those

⁴ MPEP 2111.02 “If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention’s limitations, then the preamble is not considered a limitation and is of no significance to claim construction.”.

terms can be given any reasonable meaning.” *Young v. Lumenis, Inc.*, 492 F.3d 1336, 1346 (Fed. Cir. 2007) (quoting *Datamize, LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1347 (Fed. Cir. 2005)). In other words, an indefiniteness inquiry “requires a determination whether those skilled in the art would understand what is claimed.” *Id.*

Moreover, it is well established that a claim cannot be invalid for indefiniteness if its antecedent basis is present by implication. *Cross Med. Prods., Inc. v. Medtronic Sofamor Danek, Inc.*, No. 05-1043, 2005 WL 2403777, at 23 (Fed. Cir. 2005) (citing *Slimfold Mfg. Co. v. Kinkead Indus.*, Inc., 810 F.2d 1113, 1116 (Fed. Cir. 1987)).

The Applicants submit that because the terms in question have support which is either explicit (i.e., in the case of “the candidate agents”), implicit (in the case of “the nucleic acid”) or are used in phrases which have a readily understood meaning (e.g., in the case of “the basis” and “in the absence of”), the Applicants submit that the use of the term “the” in the claims does not render the claims indefinite.

Physiological signals

Claim 38 is rejected as being “vague and indefinite as to the physiological signal the population of cells is subjected thereto given that the cells are grown *in vitro*(?)”.

Examples of physiological signals that could be used in the method are described on page 10, lines 1-2 and on page 34, lines 1-10. Given these examples, the ordinary meaning of the term “physiological signals” and the fact that the exemplary signals listed in the specification can readily be applied to cells grown *in vitro*, the use of the term “physiological signals”, as used in claim 38, should not be confusing.

“Other” cells

Claim 38 is rejected as being “vague and indefinite as to the “other” cells.

Claim 38 has been amended to cancel the term “other” and, as such, it is understood that this rejection has been addressed and may be withdrawn.

“At least one optical property”

Claim 40 is “vague and indefinite in the recitation of at least one optical property selection when the base claim recites at least three as a minimum”.

Applicants submit that there is no inconsistency in claim 40. Claim 37 requires the use of at least three parameters. Claim 40 requires that at least one of the parameters used in claim 37 is selected from “light scattering, and fluorescent dye uptake, fluorescent dye release and binding of a fluorescent antibody”.

Withdrawal of this rejection is requested.

Rejection under 35 U.S.C. § 103 – Uhr

Claims 37, 40 and 42-43 are rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Uhr (U.S. patent 5,612,185).

According to the Examiner, “Uhr, alone, discloses or teaches all the elements of the claim except the sequencing of the candidate agents.” Applicants respectfully disagree.

Uhr discloses a process for treating cancer by arresting the growth of tumor cells by placing them in cell cycle arrest (col. 2, lines 62-65). Uhr also discloses that cell cycle arrest may be induced by gene therapy, e.g., by introducing nucleic acid encoding c-fos or c-jun directly into tumor cells (col. 22, lines 6-10). Uhr also contemplates the use of retroviral vectors (col. 22, lines 14-19), and the production of transgenic mice (col. 22, lines 48-50). Uhr also allegedly discloses analyzing, by FACS, the spleens of mice into which cells have been transplanted (col. 2, lines 64-65).

Uhr’s disclosure is deficient for a number of reasons. For example:

a) Uhr does not teach the use of a library of *at least 10³ vectors encoding different candidate agents*, as required by the rejected claims. Uhr describes the use of a vector that encodes c-jun or c-fos into cells to induce cell cycle arrest. These proteins were chosen by Uhr because they are thought to induce cell cycle arrest. Thus, at best, Uhr suggests a method that employs one of two vectors (which encode c-jun or c-fos). Based on Uhr’s disclosure, there would be no reason to use more than two different vectors, let alone at least 1,000 vectors as required by the rejected claims.

In the Office Action, the Examiner argues Fig. 3 evidences that that Uhr teaches a library of at least 10^3 vectors. However, as explained in col. 17 lines 46-67, Fig. 3 is simply an RT-PCR assay of BCL₁ and CCALC cells. mRNA was made from cells, and the mRNA was assayed for the expression of myc, fos and β -actin. Uhr's Fig. 3 provides no evidence that Uhr discloses "a library of at least 10^3 vectors encoding different candidate agents" much less introducing such a library into a population of mammalian cells grown *in vitro*.

In the Office Action, the Examiner also argues that because Uhr refer to gene in the plural, i.e., states that "DNA encoding key genes such as, for example, c-fos or c-jun, may be applied directly to cells...." (Uhr, col. 22; emphasis added by the Examiner), then Uhr teaches the use of a library of at least 10^3 vectors. However, put into context (see below) that sentence merely states that cell cycle arrest can be induced by gene therapy using, e.g., fos *or* jun.

Ultimately, it is contemplated that tumor cell cycle arrest may be induced by gene therapy. DNA encoding key genes in this process, such as, for example, c-fos or c-jun, may be applied directly to cells, in the form of oligonucleotides, or other genetic constructs. It has been shown that oligonucle-

Because: a) gene therapy usually uses single genes (not "a library of at least 10^3 vectors encoding different candidate agents", as required by the claims) and b) Uhr refers to fos and jun in the alternative (i.e., using the word "or") it is clear that Uhr neither teaches or suggests the use of a library of at least 10^3 vectors encoding different candidate agents", as required by the claims.

b) Uhr does not introduce candidate agents into cells *and* subject the cells to a physiological signal as separate events, as required by the rejected claims. Uhr merely introduces compounds (c-jun or c-fos) into cells to induce cell cycle arrest. At best, the compounds can either be considered candidate agents (in which case there is no separate physiological stimulus) or as physiological stimuli (in which case there is no candidate agent). Either way, introducing candidate agents into cells *and* subjecting the cells to a physiological signal as separate events is not disclosed by Uhr. Moreover, since the general

goal of Uhr's method is to identify compounds that induce cell cycle arrest, at best Uhr teaches an assay that involves no more than determining whether a compound causes a cell to arrest. That is not the method being claimed.

In the Office Action, the Examiner argues that introducing of the candidate agents into cells *and* subjecting the cells to a physiological signal did not have to be separate events. To the extent that the claims were not clear on this matter, they have been amended to make it clear that the introducing of the candidate agents into cells and subjecting the cells to a physiological signal are done as separate events.

c) Uhr does not disclose using FACS to examine the individual cells in the cell population that has been grown *in vitro*. The only FACS methods described in Uhr's disclosure are those in which the cells of spleens of animals are examined. Such cells are grown *in vivo* rather than *in vitro* and, as such, this element of the claims is not provided.

In the Office Action, the Examiner argues that cells grown *in vitro* are described in Example 4 of the specification, e.g., in col 31 (see below).

To allow the more rapid development of further work, the inventors have established a BCL₁ line, 3B3, that replicates every three days *in vitro* and which is tumorigenic. This particular cell line grows slightly faster than *in vivo* passaged BCL₁ but is fully susceptible to induction of dormancy when BCL₁ is injected into either Id-immune or SCID mice receiving rabbit anti-Id antibody. The 3B3 *in vitro* cell line will be especially useful for investigating the kinetics of gene induction following anti-Ig treatment, and will facilitate the introduction of DNA constructs, by transfection and subsequent selection, to investigate the role of oncogene expression in dormancy induction.

However, *in vitro* cells described in this passage are not analyzed by FACS. Rather, they are injected into mice. See, e.g., the following paragraph col. 31, lines 49-64. There is no indication that the cells described in the above paragraph are examined by FACS, as discussed above.

d) Uhr does not disclose sequencing the nucleic acid encoding the candidate agent in a cell that has an altered phenotype. Since the identities of Uhr's clones (which, at best would

encode c-jun or c-fos) would be known before any experiments were initiated, there would be no need for this step to be performed.

Applicants have provided alternative support for the sequencing step of the claimed method. If the Applicants correctly understand the logic behind this rejection, this rejection can now be withdrawn.

Claims 38 and 39 are rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Uhr in view of Hide.

Hide is cited solely to provide a FACS-based method for assaying a population of cells that have been stimulated by Ca⁺⁺ or ionomycin.

However, none of Uhr's deficiencies discussed above is met by Hide's disclosure and, as such, taken in any combination, Uhr and Hide fail to teach or suggest all of the elements of the rejected claims.

Withdrawal of this rejection is therefore requested.

Claim 43 is rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Uhr in view of Conneally.

Conneally is cited solely to provide the subject matter of claim 43, i.e., a suggestion to use retroviral vectors. However, none of Uhr's deficiencies discussed above is met by Conneally's suggestion to use retroviral vectors and, as such, taken in any combination, Uhr and Conneally fails to teach or suggest all of the elements of the rejected claims.

Withdrawal of this rejection is therefore requested.

Rejection under 35 U.S.C. § 103 – Nolan in view of Jia-Ping and Uhr

Claims 37 and 40-44 are rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Nolan (WO 97/27212) in view of Jia-Ping and Uhr. Claims 38 and 39 are rejected under 35 U.S.C. § 103 as unpatentable over Nolan in view of Jia-Ping, Uhr and Hide.

These rejections are predicated on the claims not being supported by earlier filed application serial no. 09/062,330, now issued as U.S. patent 6,897,031.

The claims are submitted to be fully supported in the instant application and in parent application serial no. 09/062,330, now issued as U.S. patent 6,897,031. As such, the Examiner is requested to reconsider this rejection in view of the arguments and arguments set forth above, the Fisher declaration and the arguments presented in the prior response.

Withdrawal of this rejection is respectfully requested.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number RIGL-036CIP.

Respectfully submitted,
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